

# What About the Pill?

## Do the Possible Dangers of the Drug Exceed Natural Risks of Childbirth

By Joshua Lederberg

THE SAFETY OF the pill has been studied by a distinguished advisory group commissioned by the Food and Drug Administration. Its report over the signature of chairman Dr. Lou Hellman was headlined throughout the country on Aug. 15.

Having once enjoyed serving with Dr. Hellman on another committee, I looked forward to seeing his temper and wisdom in the full text of the report. I also hoped that it might clear up the confusion and contradictions which permeated the news accounts interpreting the report.

The published interpretations have ranged from direct approval to a Scotch verdict: "Guilt not proven." Allegations that the report offered an "amber light" go ahead must not be very helpful to women or their physicians who have reserved judgment about use of the pill.

Well over five million women in the United States are using chemical contraceptives. This means that more women at any one time are under the influence of a chemically induced pseudo-pregnancy than are actually undergoing natural pregnancy.

The report itself is much less glib than the newspaper accounts in its assessment of a complex problem. "The committee finds no adequate scientific data, at this time, proving these compounds unsafe for human use. It has nevertheless taken full cognizance of certain very infrequent but serious side effects and of possible theoretic risks suggested by animal experimental data and by some of the metabolic changes in human beings.

"In the final analysis, each physician must evaluate the advantages and the risks of this method of contraception

in comparison with other available methods or with no contraception at all. He can do this wisely only when there is presented to him dispassionate scientific knowledge of the available data."

### Science and Man

EACH PHYSICIAN does indeed carry the moral and legal responsibility to evaluate the benefits and risks of the pill for his individual patients. Above all, he must examine his patient for concurrent disease that might contraindicate the use of the pill and she must also be tested for the possibility of various side effects, most of which are more subjectively unpleasant than medically dangerous.

On the other hand, it is quite doubtful that most physicians have the necessary scientific background to reach a wiser decision than the experts have been able to do. In so controversial a field, it is especially difficult to assure the neutralization of social or religious judgments which should have nothing to do with the evaluation of the safety of these techniques.

These judgments about the pill are confounded precisely because it is not a life-saving drug directed against traditionally mortal disease for which there is no alternative remedy. To this extent, the physician's and the patient's attitudes about pregnancy, and the value attached to convenient methods of security against it, are bound to influence the level of risk regarded as acceptable.

Nowhere in the main text of the report is there an explicit mention of the risks connected with the pregnancies potentially averted or postponed by the use of the pill. However, one of the most striking statistical remarks is the guess that one million pregnancies are terminated each year by illegal abortion (compared to about four million live births).

The medical hazards connected with such illegal operations are quite unknown statistically, for obvious reasons, but it is difficult to believe that these operations are even nearly as safe as full maternity. The care of the pregnant woman is one of the outstanding accomplishments of medical progress during the past 50 years, but even today pregnancy carries a risk of 300 maternal deaths per million gestations. This number is at least 20 times higher than for any specific side effects that might conceivably be attributed to the pill by interpretation of the existing statistics.

SINCE CHANCES of deaths per million are perhaps beyond the comprehension that ordinary experience gives us, it might help to point out that one per million is approximately the risk of being killed in the course of a 40-mile automobile trip or a 500-mile air trip. (This remark is not intended as a mitigation of possible hazards. Any avoidable risk that came even close to what we unaccountably tolerate in traffic hazards would be a disgrace of judgment.)

Before turning to the findings of the committee, we must first consider what they could possibly hope to discover from examination of existing data. The medical use of contraceptive drugs was first approved by the FDA on the basis of experience with some few hundred or thousand women, which showed no important evidence of major acute toxicity. This work had in turn been preceded by extensive animal studies in order to justify the first clinical trials.

Over a period of observation of a few years, chemical contraception was then certainly safer than pregnancy. This does not dignify the pill with "absolute safety," a concept which is a delusion of the same genus as "absolute security" in world politics, or "zero residues" of pesticides in agricultural practice.

There can be no operational criterion for these absolute ideas. The committee could however scrutinize the available data for any significant increase in deaths or serious illnesses in specific categories that might be associated with taking the pill. They would then have to analyze the data to determine whether the differences, if any, in the observed numbers were statistically significant, on the one hand, or could be attributed to mere chance variation on the other.

The absolute numbers of women in question are rather small, and this certainly does intensify the difficulties of statistical evaluation.

A MUCH MORE important problem is that of knowing just what population is exposed to the pill and how it compares with the over-all population from which the mortality and disease statistics are taken. Most diseases show considerable variation in their incidence with respect to age and sex, and often with respect to socioeconomic conditions and geography.

Furthermore, the physician must decide on the general health of his patient before prescribing the pill. This inevitably introduces another bias in the characteristics of pill-users compared to the rest of the population. Mortality statistics on specific diseases are as a whole not very reliable, but at least we can look at the entire population of the United States as a reasonable statistical base.

On the other hand, the way in which medical records are kept and processed makes it difficult to be sure which women have been exposed to contraceptive drugs. Over the past few years, there have been any number of alarming claims about a superincidence of certain medical conditions among pill-taking women. None of these isolated observations is statistically conclusive, but they do indicate where the focus of attention should be placed.

There is a proper and obvious human motive in calling to attention any unexpected clustering or other hint of apparent drug-induced disease, but it is a virtual certainty that even an absolutely safe drug, if there were such a thing, would provoke many isolated observations of this kind.